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1600

RAW SEQUENCE LISTING   DATE: 03/13/2003
PATENT APPLICATION: US/09/910,186B   TIME: 15:08:51

Input Set : A:\09910186SubSeqList.txt
Output Set: N:\CRF4\03132003\I910186B.raw

```
      1 <110> APPLICANT: Smith, Leonard A.
      2        Byrne, Michael P.
      3        Middlebrook, John L.
      4        Lapenotiere, Hugh
      5        Clayton, Michael A.
      6      · Brown, Douglas R.
      8 <120> TITLE OF INVENTION: RECOMBINANT VACCINE AGAINST BOTULINUM
      9        NEUROTOXIN
     11 <130> FILE REFERENCE: A33626-A 067252.0107
C--> 13 <140> CURRENT APPLICATION NUMBER: US/09/910,186B
C--> 14 <141> CURRENT FILING DATE: 2001-07-20
     16 <150> PRIOR APPLICATION NUMBER: PCT/US00/12890
     17 <151> PRIOR FILING DATE: 2000-05-12
     19 <150> PRIOR APPLICATION NUMBER: 60/133,865
     20 <151> PRIOR FILING DATE: 1999-05-12
     22 <150> PRIOR APPLICATION NUMBER: 60/133,866
     23 <151> PRIOR FILING DATE: 1999-05-12
     25 <150> PRIOR APPLICATION NUMBER: 60/133,867
     26 <151> PRIOR FILING DATE: 1999-05-12
     28 <150> PRIOR APPLICATION NUMBER: 60/133,868
     29 <151> PRIOR FILING DATE: 1999-05-12
     31 <150> PRIOR APPLICATION NUMBER: 60/133,869
     32 <151> PRIOR FILING DATE: 1999-05-12
     34 <150> PRIOR APPLICATION NUMBER: 60/146,192
     35 <151> PRIOR FILING DATE: 1999-07-29
     37 <160> NUMBER OF SEQ ID NOS: 42
     39 <170> SOFTWARE: FastSEQ for Windows Version 4.0
     41 <210> SEQ ID NO: 1
     42 <211> LENGTH: 1332
     43 <212> TYPE: DNA
     44 <213> ORGANISM: Artificial Sequence
     46 <220> FEATURE:
     47 <223> OTHER INFORMATION: Synthetic construct based on BoNTA Hc
W--> 49 <221> NAME/KEY: CDS
     50 <222> LOCATION: (13)...(1326)
W--> 52 <400> 1
     53 gaattcgaaa cg atg cgt ctg ctg tct acc ttc act gaa tac atc aag aac 51
     54               Met Arg Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys Asn
     55                1               5                     10
     57 atc atc aat acc tcc atc ctg aac ctg cgc tac gaa tcc aat cac ctg   99
     58 Ile Ile Asn Thr Ser Ile Leu Asn Leu Arg Tyr Glu Ser Asn His Leu
     59       15                20                    25
     61 atc gac ctg tct cgc tac gct tcc aaa atc aac atc ggt tct aaa gtt  147
```

```
62 Ile Asp Leu Ser Arg Tyr Ala Ser Lys Ile Asn Ile Gly Ser Lys Val
63    30                35                40                45
65 aac ttc gat ccg atc gac aag aat cag atc cag ctg ttc aat ctg gaa   195
66 Asn Phe Asp Pro Ile Asp Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu
67                50                55                60
69 tct tcc aaa atc gaa gtt atc ctg aag aat gct atc gta tac aac tct   243
70 Ser Ser Lys Ile Glu Val Ile Leu Lys Asn Ala Ile Val Tyr Asn Ser
71                65                70                75
73 atg tac gaa aac ttc tcc acc tcc ttc tgg atc cgt atc ccg aaa tac   291
74 Met Tyr Glu Asn Phe Ser Thr Ser Phe Trp Ile Arg Ile Pro Lys Tyr
75             80                85                90
77 ttc aac tcc atc tct ctg aac aat gaa tac acc atc atc aac tgc atg   339
78 Phe Asn Ser Ile Ser Leu Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met
79         95                100               105
81 gaa aac aat tct ggt tgg aaa gta tct ctg aac tac ggt gaa atc atc   387
82 Glu Asn Asn Ser Gly Trp Lys Val Ser Leu Asn Tyr Gly Glu Ile Ile
83 110               115               120               125
85 tgg act ctg cag gac act cag gaa atc aaa cag cgt gtt gta ttc aaa   435
86 Trp Thr Leu Gln Asp Thr Gln Glu Ile Lys Gln Arg Val Val Phe Lys
87               130               135               140
89 tac tct cag atg atc aac atc tct gac tac atc aat cgc tgg atc ttc   483
90 Tyr Ser Gln Met Ile Asn Ile Ser Asp Tyr Ile Asn Arg Trp Ile Phe
91             145               150               155
93 gtt acc atc acc aac aat cgt ctg aat aac tcc aaa atc tac atc aac   531
94 Val Thr Ile Thr Asn Asn Arg Leu Asn Asn Ser Lys Ile Tyr Ile Asn
95         160               165               170
97 ggc cgt ctg atc gac cag aaa ccg atc tcc aat ctg ggt aac atc cac   579
98 Gly Arg Leu Ile Asp Gln Lys Pro Ile Ser Asn Leu Gly Asn Ile His
99     175               180               185
101 gct tct aat aac atc atg ttc aaa ctg gac ggt tgt cgt gac act cac   627
102 Ala Ser Asn Asn Ile Met Phe Lys Leu Asp Gly Cys Arg Asp Thr His
103 190               195               200               205
105 cgc tac atc tgg atc aaa tac ttc aat ctg ttc gac aaa gaa ctg aac   675
106 Arg Tyr Ile Trp Ile Lys Tyr Phe Asn Leu Phe Asp Lys Glu Leu Asn
107               210               215               220
109 gaa aaa gaa atc aaa gac ctg tac gac aac cag tcc aat tct ggt atc   723
110 Glu Lys Glu Ile Lys Asp Leu Tyr Asp Asn Gln Ser Asn Ser Gly Ile
111             225               230               235
113 ctg aaa gac ttc tgg ggt gac tac ctg cag tac gac aaa ccg tac tac   771
114 Leu Lys Asp Phe Trp Gly Asp Tyr Leu Gln Tyr Asp Lys Pro Tyr Tyr
115         240               245               250
117 atg ctg aat ctg tac gat ccg aac aaa tac gtt gac gtc aac aat gta   819
118 Met Leu Asn Leu Tyr Asp Pro Asn Lys Tyr Val Asp Val Asn Asn Val
119     255               260               265
121 ggt atc cgc ggt tac atg tac ctg aaa ggt ccg cgt ggt tct gtt atg   867
122 Gly Ile Arg Gly Tyr Met Tyr Leu Lys Gly Pro Arg Gly Ser Val Met
123 270               275               280               285
125 act acc aac atc tac ctg aac tct tcc ctg tac cgt ggt acc aaa ttc   915
126 Thr Thr Asn Ile Tyr Leu Asn Ser Ser Leu Tyr Arg Gly Thr Lys Phe
```

RAW SEQUENCE LISTING
PATENT APPLICATION: **US/09/910,186B**

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```
127                   290                   295                   300
129 atc atc aag aaa tac gcg tct ggt aac aag gac aat atc gtt cgc aac      963
130 Ile Ile Lys Lys Tyr Ala Ser Gly Asn Lys Asp Asn Ile Val Arg Asn
131               305                   310                   315
133 aat gat cgt gta tac atc aat gtt gta gtt aag aac aaa gaa tac cgt      1011
134 Asn Asp Arg Val Tyr Ile Asn Val Val Val Lys Asn Lys Glu Tyr Arg
135               320                   325                   330
137 ctg gct acc aat gct tct cag gct ggt gta gaa aag atc ttg tct gct      1059
138 Leu Ala Thr Asn Ala Ser Gln Ala Gly Val Glu Lys Ile Leu Ser Ala
139               335                   340                   345
141 ctg gaa atc ccg gac gtt ggt aat ctg tct cag gta gtt gta atg aaa      1107
142 Leu Glu Ile Pro Asp Val Gly Asn Leu Ser Gln Val Val Val Met Lys
143 350                   355                   360                   365
145 tcc aag aac gac cag ggt atc act aac aaa tgc aaa atg aat ctg cag      1155
146 Ser Lys Asn Asp Gln Gly Ile Thr Asn Lys Cys Lys Met Asn Leu Gln
147               370                   375                   380
149 gac aac aat ggt aac gat atc ggt ttc atc ggt ttc cac cag ttc aac      1203
150 Asp Asn Asn Gly Asn Asp Ile Gly Phe Ile Gly Phe His Gln Phe Asn
151               385                   390                   395
153 aat atc gct aaa ctg gtt gct tcc aac tgg tac aat cgt cag atc gaa      1251
154 Asn Ile Ala Lys Leu Val Ala Ser Asn Trp Tyr Asn Arg Gln Ile Glu
155               400                   405                   410
157 cgt tcc tct cgc act ctg ggt tgc tct tgg gag ttc atc ccg gtt gat      1299
158 Arg Ser Ser Arg Thr Leu Gly Cys Ser Trp Glu Phe Ile Pro Val Asp
159               415                   420                   425
161 gac ggt tgg ggt gaa cgt ccg ctg taa gaattc                          1332
162 Asp Gly Trp Gly Glu Arg Pro Leu  *
163 430                   435
166 <210> SEQ ID NO: 2
167 <211> LENGTH: 437
168 <212> TYPE: PRT
169 <213> ORGANISM: Artificial Sequence
171 <220> FEATURE:
172 <223> OTHER INFORMATION: Encoded polypeptide of a synthetic construct based
173      on BoNTA Hc
175 <400> SEQUENCE: 2
176 Met Arg Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys Asn Ile Ile Asn
177 1                 5                   10                  15
178 Thr Ser Ile Leu Asn Leu Arg Tyr Glu Ser Asn His Leu Ile Asp Leu
179       ?       20                  25                  30
180 Ser Arg Tyr Ala Ser Lys Ile Asn Ile Gly Ser Lys Val Asn Phe Asp
181           35                  40                  45
182 Pro Ile Asp Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu Ser Ser Lys
183       50                  55                  60
184 Ile Glu Val Ile Leu Lys Asn Ala Ile Val Tyr Asn Ser Met Tyr Glu
185 65                  70                  75                  80
186 Asn Phe Ser Thr Ser Phe Trp Ile Arg Ile Pro Lys Tyr Phe Asn Ser
187               85                  90                  95
188 Ile Ser Leu Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Glu Asn Asn
```

```
189                100                    105                    110
190  Ser Gly Trp Lys Val Ser Leu Asn Tyr Gly Glu Ile Ile Trp Thr Leu
191           115                120               125
192  Gln Asp Thr Gln Glu Ile Lys Gln Arg Val Val Phe Lys Tyr Ser Gln
193           130                135               140
194  Met Ile Asn Ile Ser Asp Tyr Ile Asn Arg Trp Ile Phe Val Thr Ile
195  145                 150               155                    160
196  Thr Asn Asn Arg Leu Asn Asn Ser Lys Ile Tyr Ile Asn Gly Arg Leu
197                165                170                    175
198  Ile Asp Gln Lys Pro Ile Ser Asn Leu Gly Asn Ile His Ala Ser Asn
199                180                185                    190
200  Asn Ile Met Phe Lys Leu Asp Gly Cys Arg Asp Thr His Arg Tyr Ile
201           195                200               205
202  Trp Ile Lys Tyr Phe Asn Leu Phe Asp Lys Glu Leu Asn Glu Lys Glu
203     210                215               220
204  Ile Lys Asp Leu Tyr Asp Asn Gln Ser Asn Ser Gly Ile Leu Lys Asp
205  225                 230               235                    240
206  Phe Trp Gly Asp Tyr Leu Gln Tyr Asp Lys Pro Tyr Tyr Met Leu Asn
207                245                250                    255
208  Leu Tyr Asp Pro Asn Lys Tyr Val Asp Val Asn Asn Val Gly Ile Arg
209                260                265                    270
210  Gly Tyr Met Tyr Leu Lys Gly Pro Arg Gly Ser Val Met Thr Thr Asn
211           275                280               285
212  Ile Tyr Leu Asn Ser Ser Leu Tyr Arg Gly Thr Lys Phe Ile Ile Lys
213     290                295               300
214  Lys Tyr Ala Ser Gly Asn Lys Asp Asn Ile Val Arg Asn Asn Asp Arg
215  305                 310               315                    320
216  Val Tyr Ile Asn Val Val Val Lys Asn Lys Glu Tyr Arg Leu Ala Thr
217                325                330                    335
218  Asn Ala Ser Gln Ala Gly Val Glu Lys Ile Leu Ser Ala Leu Glu Ile
219           340                345               350
220  Pro Asp Val Gly Asn Leu Ser Gln Val Val Val Met Lys Ser Lys Asn
221           355                360               365
222  Asp Gln Gly Ile Thr Asn Lys Cys Lys Met Asn Leu Gln Asp Asn Asn
223           370                375               380
224  Gly Asn Asp Ile Gly Phe Ile Gly Phe His Gln Phe Asn Asn Ile Ala
225  385.                390                395                    400
226  Lys Leu Val Ala Ser Asn Trp Tyr Asn Arg Gln Ile Glu Arg Ser Ser
227                405                410                    415
228  Arg Thr Leu Gly Cys Ser Trp Glu Phe Ile Pro Val Asp Asp Gly Trp
229           420                425               430
230  Gly Glu Arg Pro Leu
231           435
234  <210> SEQ ID NO: 3
235  <211> LENGTH: 1323
236  <212> TYPE: DNA
237  <213> ORGANISM: Artificial Sequence
239  <220> FEATURE:
240  <223> OTHER INFORMATION: Synthetic construct based on BoNTA Hc
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```
                    RAW SEQUENCE LISTING            DATE: 03/13/2003
                    PATENT APPLICATION: US/09/910,186B    TIME: 15:08:51

                    Input Set : A:\09910186SubSeqList.txt
                    Output Set: N:\CRF4\03132003\I910186B.raw
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W--> 242 <221> NAME/KEY: CDS
     243 <222> LOCATION: (13)...(1314)
W--> 245 <400> 3

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246 gaattcgaaa cg atg tct acc ttc act gaa tac atc aag aac atc atc aat 51
247                Met Ser Thr Phe Thr Glu Tyr Ile Lys Asn Ile Ile Asn
248                 1               5                  10
250 acc tcc atc ctg aac ctg cgc tac gaa tcc aat cac ctg atc gac ctg 99
251 Thr Ser Ile Leu Asn Leu Arg Tyr Glu Ser Asn His Leu Ile Asp Leu
252     15                  20                  25
254 tct cgc tac gct tcc aaa atc aac atc ggt tct aaa gtt aac ttc gat 147
255 Ser Arg Tyr Ala Ser Lys Ile Asn Ile Gly Ser Lys Val Asn Phe Asp
256 30                  35                  40                  45
258 ccg atc gac aag aat cag atc cag ctg ttc aat ctg gaa tct tcc aaa 195
259 Pro Ile Asp Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu Ser Ser Lys
260                 50                  55                  60
262 atc gaa gtt atc ctg aag aat gct atc gta tac aac tct atg tac gaa 243
263 Ile Glu Val Ile Leu Lys Asn Ala Ile Val Tyr Asn Ser Met Tyr Glu
264                 65                  70                  75
266 aac ttc tcc acc tcc ttc tgg atc cgt atc ccg aaa tac ttc aac tcc 291
267 Asn Phe Ser Thr Ser Phe Trp Ile Arg Ile Pro Lys Tyr Phe Asn Ser
268         80                  85                  90
270 atc tct ctg aac aat gaa tac acc atc atc aac tgc atg gaa aac aat 339
271 Ile Ser Leu Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Glu Asn Asn
272     95                  100                 105
274 tct ggt tgg aaa gta tct ctg aac tac ggt gaa atc atc tgg act ctg 387
275 Ser Gly Trp Lys Val Ser Leu Asn Tyr Gly Glu Ile Ile Trp Thr Leu
276 110                 115                 120                 125
278 cag gac act cag gaa atc aaa cag cgt gtt gta ttc aaa tac tct cag 435
279 Gln Asp Thr Gln Glu Ile Lys Gln Arg Val Val Phe Lys Tyr Ser Gln
280                 130                 135                 140
282 atg atc aac atc tct gac tac atc aat cgc tgg atc ttc gtt acc atc 483
283 Met Ile Asn Ile Ser Asp Tyr Ile Asn Arg Trp Ile Phe Val Thr Ile
284                 145                 150                 155
286 acc aac aat cgt ctg aat aac tcc aaa atc tac atc aac ggc cgt ctg 531
287 Thr Asn Asn Arg Leu Asn Asn Ser Lys Ile Tyr Ile Asn Gly Arg Leu
288         160                 165                 170
290 atc gac cag aaa ccg atc tcc aat ctg ggt aac atc cac gct tct aat 579
291 Ile Asp Gln Lys Pro Ile Ser Asn Leu Gly Asn Ile His Ala Ser Asn
292     175                 180                 185
294 aac atc atg ttc aaa ctg gac ggt tgt cgt gac act cac cgc tac atc 627
295 Asn Ile Met Phe Lys Leu Asp Gly Cys Arg Asp Thr His Arg Tyr Ile
296 190                 195                 200                 205
298 tgg atc aaa tac ttc aat ctg ttc gac aaa gaa ctg aac gaa aaa gaa 675
299 Trp Ile Lys Tyr Phe Asn Leu Phe Asp Lys Glu Leu Asn Glu Lys Glu
300                 210                 215                 220
302 atc aaa gac ctg tac gac aac cag tcc aat tct ggt atc ctg aaa gac 723
303 Ile Lys Asp Leu Tyr Asp Asn Gln Ser Asn Ser Gly Ile Leu Lys Asp
304                 225                 230                 235
306 ttc tgg ggt gac tac ctg cag tac gac aaa ccg tac tac atg ctg aat 771
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VERIFICATION SUMMARY   DATE: 03/13/2003
PATENT APPLICATION: **US/09/910,186B**   TIME: 15:08:52

Input Set : **A:\09910186SubSeqList.txt**
Output Set: **N:\CRF4\03132003\I910186B.raw**

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L:13 M:270 C: Current Application Number differs, Replaced Current Application Number
L:14 M:271 C: Current Filing Date differs, Replaced Current Filing Date
L:49 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:52 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:242 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:245 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:3
L:435 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:438 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:5
L:628 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:631 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:7
L:821 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:824 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:9
L:1020 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:1023 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:11
L:1219 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:1222 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:13
L:1419 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:1422 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:15
L:1610 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:1613 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:17
L:1809 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:1812 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:19
L:1990 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:1993 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:21
L:2171 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:2174 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:23
L:2347 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:2350 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:25
L:2522 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:2525 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:27
L:2692 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:2695 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:29
L:2873 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:2876 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:31
L:3054 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:3057 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:33
L:3245 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:3248 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:35
L:3432 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:3435 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:37
L:3617 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:3620 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:39
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